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EXAMINER	
~~BRUMBACK, B~~ BRENDA BRUMBACK	
ART UNIT ~~1643~~	PAPER NUMBER
1643	16

DATE MAILED: ~~09/29/99~~

Below is a communication from the EXAMINER in charge of this application

COMMISSIONER OF PATENTS AND TRADEMARKS

ADVISORY ACTION

☑ THE PERIOD FOR RESPONSE:

a) ☑ is extended to run 4 months or continues to run _____ from the date of the final rejection

b) ☐ expires three months from the date of the final rejection or as of the mailing date of this Advisory Action, whichever is later. In no event however, will the statutory period for the response expire later than six months from the date of the final rejection.

Any extension of time must be obtained by filing a petition under 37 CFR 1.136(a), the proposed response and the appropriate fee. The date on which the response, the petition , and the fee have been filed is the date of the response and also the date for the purposes of determining the period of extension and the corresponding amount of the fee. Any extension fee pursuant to 37 CFR 1.17 will be calculated from the date of the originally set shortened statutory period for response or as set forth in b) above.

☐ Appellant's Brief is due in accordance with 37 CFR 1.192(a).

☑ Applicant's response to the final rejection, filed 09/07/99 has been considered with the following effect, but it is not deemed to place the application in condition for allowance:

1. ☑ The proposed amendments to the claim and /or specification will not be entered and the final rejection stands because: filed in the Supplemental Amendment After Final

a. ☐ There is no convincing showing under 37 CFR 1.116(b) why the proposed amendment is necessary and was not earlier presented.

b. ☑ They raise new issues that would require further consideration and/or search. (See Note).

c. ☐ They raise the issue of new matter. (See Note).

d. ☑ They are not deemed to place the application in better form for appeal by materially reducing or simplifying the issues for appeal.

e. ☑ They present additional claims without cancelling a corresponding number of finally rejected claims.

NOTE: See attached.

2. ☐ Newly proposed or amended claims _____ would be allowed if submitted in a separately filed amendment cancelling the non-allowable claims.

3. ☑ Upon the filing an appeal, the proposed amendment ☐ will be entered ☑ will not be entered and the status of the claims will be as follows:

Claims allowed: _____

Claims objected to: _____

Claims rejected: 5, 6, 8, 10, 11, 15, 16, 19, 26-30, 32-41, 43, 44, 46, 48-52, and 55-101

However;

☑ Applicant's response has overcome the following rejection(s): The rejection of claims 6, 31, 32, and 33 under 34USC 102(b) as anticipated by Madore et al., and the rejection of claims 5, 8, 10, 11, 30, 38, 49, 55, 60, 61-65 and 72-100 under 35USC 112, 1st paragraph for recitation of "plate".

4. ☑ The affidavit, exhibit or request for reconsideration has been considered but does not overcome the rejection because: See attached

5. ☐ The affidavit or exhibit will not be considered because applicant has not shown good and sufficent reasons why it was not earlier presented.

☐ The proposed drawing correction ☐ has ☐ has not been approved by the examiner.

☐ Other

DETAILED ACTION

Attachment to Advisory Action

1. The Request for Withdrawal of Finality filed 06/14/99 has been entered as Paper # 12. The Amendment After Final filed 09/07/99 has been entered as Paper # 14. The Supplemental Amendment After Final filed 09/07/99 has not been entered for the reasons outlined *supra*.

2. Pending claims are 5, 6, 8, 10, 11, 15, 16, 19, 26-30, 32-41, 43, 44, 46, 48-52, and 55-101. Claims 5, 6, 8, 10, 11, 15, 16, 19, 26-30, 32-41, 43, 44, 46, 48-52, and 55-101 stand rejected.

Request for Withdrawal of Finality

3. Applicant's arguments presented in Paper # 12 have been fully considered but are not persuasive for the following reasons. Applicant argues that the finality of the Office Action mailed 05/04/99 (Paper # 11) should be withdrawn because the examiner introduced new grounds of rejection. This is not found persuasive because the examiner finds no new grounds that were introduced in Paper # 11.

Applicant alleges that the response to argument made in paragraph 4(a) of Paper # 11 was "in effect ... a scope rejection" that was "a new ground of rejection". This argument is not found persuasive and is not completely understood, because the original rejection made in Paper # 7 was a "scope" rejection based on a lack of enablement for the broad scope of the claims. In Paper #7,

the examiner rejected the claims as lacking enablement for the wide range of immunogens claimed (which include a number of viral antigens, as well as bacterial antigens) based on data generated solely from anthrax and diphtheria (bacterial) antigens (see Paper # 7, paragraph 4, lines 14-21). The examiners comments quoted by the applicant speak directly to the original grounds of rejection and raise no new grounds.

Applicant also alleges that the examiner made a new scope rejection in paragraph 4(b) in Paper # 11. Once again, this paragraph speaks directly to applicant's argument regarding enablement for the broad scope of the claims and the suggestion of effectiveness of other immunogens based on data from BCG and smallpox and raises no new grounds of rejection.

In response to applicant's allegation that paragraph 4(i) in Paper # 11 raises a new grounds of rejection, this paragraph outlines the reasons why the examiner found applicant's arguments regarding extrapolation of mouse and rat model data to humans to be nonpersuasive. The issue of difference in maturation rates between the rodent models and humans is but one of the myriad of factors to be considered in extrapolation of rodent data to humans, where subject age at the time of immunization is a critical limitation. The original rejection was based on a lack of enablement in the specification for mammals other than rodents (see page 5 line 13, through page 6, line 6 of Paper # 7). Once again, the examiner's comments speak directly to the original grounds of rejection and raise no new grounds.

Applicant's rationale for alleging that a new grounds of rejection was raised based indefiniteness is not understood. The original rejection in Paper # 7 was made under 35 U.S.C.

112, second paragraph, wherein it was stated that the claim was rejected "as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention" (see page 7 of Paper # 7). The statement "other than BCG is not a positive limitation" delineates that phrase as the portion of the claim which is indefinite. The examiners comments speak directly to the original rejection. Nowhere did the examiner state that term "immunogens" in and of itself is indefinite; rather the examiner maintained that "other than BCG" is not a positive limitation because the remaining species of immunogens were not disclosed.. Thus, once again, no new issues were raised.

For these reasons, applicant's request for withdrawal of finality is not found to be persuasive, and the finality of the Office Action mailed 05/04/99 (Paper # 11) is maintained.

4. Entry of new claim 102 would raise new issues under 35 U.S.C. 112, first and second paragraphs, for recitation of maturation of a subject's immune system comparable to 42 days in a mouse or rat. The disclosure fails to teach comparable maturation rates and thus raises issues of new matter and indefiniteness.

Entry of new claims 103-105 would introduce new combinations of limitations not previously combined and would thus raise new issues requiring further search. Additionally, claim 103 recites the phrase "at specific times after birth", which has been held to be indefinite in previous rejections.

Entry of new claim 106 would introduce a new limitation (other than smallpox), which would raise a new issue and require further search. Original PCT claim 7 was not presented with the original disclosure in the instant case (see page 111 of the disclosure). Additionally, entry of claim 106 would raise a new issue of indefiniteness of "other than smallpox".

Therefore, none of the proposed new claims are entered.

5. The rejection of claims 2-17, 19, 21, 23-33, 34-55, 56-58, and 101 under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-42 of Classen U.S. Patent No. 5,728,385 and claims 1-47 of Classen U.S. Patent No. 5,723,283 is maintained. The examiner notes applicant's intention to either cancel the method claims or file a terminal disclaimer upon indication of allowable kit claims.

Claim Rejections - 35 USC § 102

6. The rejection of claims 6, 21, 32, 33, and 101 (method claims) under 34 U.S.C. 102(b) as being anticipated by Madore et al. is withdrawn. Applicant's arguments were persuasive.

7. The rejection of claims 8, 10, 11, 15, 16, 19, 26-30, 34-41, 43, 44, 46, 48-52, and 55 (kit claims) under 34 U.S.C. 102(b) as being anticipated by Madore et al.; the rejection of claims 5, 6, 8, 10, 11, 15, 16, 19, 26-30, 32-41, 43, 44, and 46-52 under 35 U.S.C. 102(b) as anticipated by Dengrove et al.; the rejection of claims 5, 6, 8, 10, 11, 15, 16, 19, 26-30, 32-41, 43, 44, and 46-

52 under 35 U.S.C. 102(b) as anticipated by Halsey et al.; and the rejection of claims 5, 6, 8, 10, 11, 15, 16, 19, 26-30, 32-41, 43, 44, and 46-52 under 35 U.S.C. 102(b) as anticipated by John 6 are all maintained. Applicant's arguments have been fully considered but they are not persuasive.

Applicant argues a functional relationship between the printed matter or labeling and the immunogens of the claimed kits which renders the kits patentable. The immunogens of the claimed kits remain functional absent the labeling; therefore no functional relationship exists between the labeling and the immunogens that would be given patentable weight. In In re Miller and In re Gulak, the function of the devices depends on the printed matter found on the substrates; without the printed indicia or numbers, the substrates lose their function. Such is not the case with the instant kits. The immunogens remain fully functionally absent the labeling.

Claim Rejections - 35 USC § 112

8. The rejection of claims 5, 6, 8, 10, 11, 15, 16, 19, and 65-101 under 35 U.S.C. 112, second paragraph, is maintained. Applicant's arguments have been fully considered but they are not persuasive.

As has been discussed previously, the rejection for indefiniteness based on "immunogen other than BCG" was based on the fact that "other than BCG" is not a positive limitation, and was not based on the use of the word "immunogen". However, in response to applicant's arguments regarding the use of the term "immunogen", the portion of the specification applicant

refers to defines an immunogen as " a class of molecules that elicit an immune response through classical immunologic pathways". This definition is so broad as to encompass any and all of a virtually limitless array of materials that have ever been used to elicit an immune response of any kind in any animal. Because of the difficulty in determining the vast plethora of embodiments, the term is so broad as to be indefinite.

The examiner disagrees with applicant's assertion that the phrase "specific times after birth" is broad, but not indefinite. Webster's II New Riverside Dictionary (at page 1116, attached hereto) defines "specific" as "set forth explicitly: definite". Recitation of "specific times after birth" without a teaching of what embodiments the recitation encompasses renders the claim indefinite. A broad recitation would be "sometime after birth" or "any time after birth" or simply "after birth".

9.. The rejection of claims 6, 32, and 101 under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention is maintained. Applicant's arguments have been fully considered but they are not persuasive. As was previously pointed out, the present application is a continuation-in-part of the parent application which issued as U.S. 5,728,385 and does not incorporate the prior case by reference; thus, citation of material in the original case which was excluded from the present case does not support the newly recited material.. Regarding

applicant's citation of original claims 1, 7, 12 and 13 in the present application, these claims were not present in the instant application at the time of filing (see page 111). These matters might be resolved if applicant were to point out where in the **present** disclosure, support for the newly recited material may be found.

10. The rejection of claims 5, 8, 10, 11, 30, 38, 49, 55, 60, 61-65, 72-100 under 35 U.S.C. 112, first paragraph, for recitation of protection is withdrawn. Applicant's arguments concerning this point were persuasive. However, the rejection is maintained for claims 5, 6, 8, 10, 11, 15, 16, 19, 26-30, 32-41, 43, 44, 46, 48-52, and 55-101 for the remaining grounds.

Applicant's arguments regarding issued patents U.S. 5,728,385 and U.S. 5,728,283 are noted; however, determination of enablement and patentability is based on the relevant statutes, on precedents set by case law, and on the particulars of each application, not on previously issued patents.

For clarification of the record, the examiner has made no assertion regarding the presence of LPS in all bacterial vaccines.

Applicant argues broadly that "the immune system does not treat viral proteins any differently than it does bacterial proteins" and that vaccines comprising viral proteins will elicit the same immune response as those of bacterial proteins. The art teaches that this is often not the case. The bacterial immunogens encompassed in the claimed invention and cited in the working examples are known vaccines of proven efficacy for eliciting an immune response. Effective

vaccines for herpes simplex virus, hepatitis C virus, human immunodeficiency virus, and cytomegalovirus, to name a few, have proven elusive. Therefore, the validity of data based on responses mounted to specific bacterial immunogens of known immunogenicity cannot be assumed to be valid for the entire range of claimed immunogens, which includes viruses for which there are no current efficacious vaccines. This was discussed in the original enablement rejection of Paper # 7. The Classen Declaration regarding prevention of diabetes in mice by administration of hepatitis B vaccine has been considered; however, it is not sufficient to overcome the rejection because this vaccine is also one of known effectiveness and immunogenicity. Applicant has provided no evidence in support of the argument that vaccines comprising proteins of any of the viruses claimed, which include viruses for which there are no known vaccines, would have the same immunogenic effect as the bacterial vaccines. As was discussed in Paper # 11, epidemiological data "suggesting" effectiveness for other immunogens is insufficient evidence to overcome the teachings of the art. The examiner has not excluded the historical and epidemiological data presented, but has merely found it inconclusive.

The examiner maintains that preventing autoimmune disease is highly unpredictable. The relevance of applicant's arguments pertaining to corticosteroids and interferons, however, is unclear. On the surface, the effects of corticosteroids and interferons on existing autoimmune disease would seem to be unrelated to prevention of the disease.

Applicant asserts that because the antidiabetic effect is not a specific immune response to diabetes-associated autoantigens, it is reasonable to expect that the same antidiabetic effect could

be achieved with many different antigens; however, applicant also states that the mode of action of this antidiabetic effect has not been established. The examiner maintains that applicant has provided no convincing evidence for this assertion.

Applicant's arguments regarding extrapolation of data from rodents to humans has been addressed in paper # 11 and *supra.* The examiner notes applicant's argument regarding the rate of maturation of the immune system in rodents compared to humans; however, the times of onset of diabetes in rodents and humans would not seem to share the same type of direct linear correlation, as the onset of diabetes in humans is after some years of maturation.

Applicant's discussion regarding the possible relationship of viral infections to the onset of autoimmune disease and diabetes is noted; however, its relevance of this discussion to the outstanding rejections is not clear.

9. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Brenda Brumback whose telephone number is (703) 306-3220. If the examiner can not be reached, inquiries can be directed to Supervisory Patent Examiner Lynette Smith whose telephone number is (703) 308-3909. Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist whose telephone number is (703) 308-0196. Papers related to this application may be submitted to Group 1600 by facsimile transmission. Papers should be faxed to Examiner Brenda Brumback, Art Unit 1643 and should be marked "OFFICIAL" for entry into prosecution history or "DRAFT" for consideration by the examiner without entry. The Art Unit 1643 FAX telephone number is (703)-305-3014. FAX machines will be available to receive transmissions 24 hours a day. In compliance with 1096 OG 30, the filing date accorded to each OFFICIAL fax transmission will be determined by the FAX machine's stamped date found on the last page of the transmission, unless that date is a Saturday, Sunday or Federal Holiday with the District of Columbia, in which case the OFFICIAL date of receipt will be the next business day.

Brenda Brumback
September 23, 1999

DONNA WORTMAN
PRIMARY EXAMINER